REMARKS

Claims 19, 20, 22-27 and 36-37 are being examined.

Applicants again request Rejoinder of claims 28-30 and 32-35. Under MPEP § 821.04, if applicant elects claims directed to the product, and a product claim is subsequently found allowable, withdrawn process claims which depend from or otherwise include all the limitations of the allowable product claim will be rejoined. Applicants assert that claims 19, 20, 22-27, and 36-37 are allowable and because the subject matter of claims 28-30 and 32-35 pertains to the same scope as the allowable claims in compliance with §821.04, these claims should be rejoined and allowed.

I. Rejection Under 35 U.S.C. § 102(b)

Claims 19, 20, 23, 27 and 36 have been rejected as anticipated by Anderson et al. (Biochem Soc. Trans. (1987) 15(4): 660-661). The Office alleges that Anderson's antibody need only "inhibit" a fraction at a ratio of 1:2.

The Office has stated that "the mAb 175-62 only inhibits CP hemolysis in the assay [referring to Figure 3] when the serum concentration in the buffer/medium is greater than 10%. At serum concentrations of less than 10%, the inhibitory ability of mAb 175-62 is greatly reduced." (Office Action at page 7.) It is clear from this statement that the Office has incorrectly interpreted the results presented in Figure 3.

The assay presented in Figure 3 shows data indicating the hemolytic activity at various serial dilutions of serum containing classical complement activity. The hemolytic assay performed involved the use of whole serum containing all of the components necessary for complement activation including 20 µg/ml (or 0.2 µM) of endogenous complement C2 component. To this serum sample, different ratios of mAb 175-62 (anti-C2) were added as described at page 18, lines 15-17.

Sample	Serum	C2 Conc.(μM)	mAb Conc (μM)	mAb:C2 Ratio
A	Whole	0.2	0.4	2:1
B	Whole	0.2	0.2	1:1
C	Whole	0.2	0.1	1:2
D	Whole	0.2	0 (saline)	NA

In Figure 3, the Applicants plotted the resulting data for Samples C and D of the table above: Sample C having a molar ratio of one antibody molecule for every two C2 molecules (1:2) and Sample D (the untreated control) with no antibody. The sample treated with mAb 175-62 was plotted as the closed circles. The control sample was treated with buffered saline and was plotted as the open squares.

After the mAb was incubated with the serum sample to allow binding of the C2, the sample was serially diluted with buffered saline and then sensitized chicken RBCs were added to assay the amount of classical complement activity remaining in the sample by measuring the amount of hemolysis of the added RBCs. As the serum becomes more and more dilute, the amount of classical pathway components present in the sample are proportionally less and therefore the % hemolysis is correspondingly less. The control shows the level of hemolysis possible at each concentration of serum in the absence of antibody. So, looking at the control plot of the open squares, one sees a dilution dependent level of hemolysis. In the control, when the serum concentration is about 50% about 70% of the RBCs are lysed. When the serum concentration is diluted to 0.1%, the amount of complement activity has been reduced below the threshold of detection.

In the treated sample, the monoclonal antibody binds C2 (in this case all of the C2) and, as a consequence, the amount of hemolysis is reduced to 0% for all dilutions[1]. If some amount of C2 had remained in the sample after addition of the mAb, then there would have been some proportionate level of hemolysis. In other words, at higher concentrations of serum, where there was a potential for more C2 to be present, one might have seen some % hemolysis. However, because the mAb 175-62 was able to bind C2 at a ratio of 1:2, all of the C2 was bound up by the antibody and the amount of hemolysis was undetectable at all concentrations of serum tested. Thus, the plot of samples containing antibody showed no dilution dependent effect, or in other words, 100% inhibition of hemolysis at **all** concentrations of serum.

Anderson et al. state in the second column, first full paragraph, last sentence, that in a standard hemolytic assay "50% inhibition of C2 hemolytic activity was achieved on addition to the serum of 7-fold molar excess of antibody over C2." [or the equivalent of 14:2] Thus, Anderson's antibody requires a ratio of at least 7 antibody molecules for every one C2 molecule, or a 14 fold greater concentration of antibody than the present invention to achieve a level of inhibition of only 50%. In contrast, Applicants achieved 100% inhibition of C2 hemolytic activity at a ratio of one antibody to two molecules of C2 (1:2). Regardless of the concentration of serum present in the hemolytic assay performed by Anderson, they were not able to achieve 50% inhibition at molar ratios of mAb to C2 less than 14:2, and thus that antibody cannot anticipate a claim to antibody having greater than 50% inhibition at a ratio of 1:2.

[1] The lowest dilution of serum feasible in this assay is 50% due to the volume of diluents, serum, and sensitized RBCs added.

II. Rejection Under 35 U.S.C. § 103(a)

A. Claims 19 and 24 have been rejected as being unpatentable over Anderson et al., in view of Janeway, Vakeva et al. and Stolzner.

In view of the discussion in Section I above, Anderson et al. do not teach an antibody capable of inhibiting complement activation greater than 50% at a ratio of 1:2. Thus, the primary reference does not provide sufficient disclosure to render the claimed invention unpatentable. Thus, Applicants request that the rejection be withdrawn.

B. Claims 19 and 22 have been rejected as being unpatentable over Anderson et al., in view of U.S. Pat. No. 5,861,156, Vakeva et al. and Stolzner.

In view of the discussion in Section I above, Anderson et al. do not teach an antibody capable of inhibiting complement activation greater than 50% at a ratio of 1:2. Thus, the primary reference does not provide sufficient disclosure to render the claimed invention unpatentable. Thus, Applicants request that the rejection be withdrawn.

II. Rejection Under 35 U.S.C. § 112, First Paragraph

Claims 19, 20, 22-24, 27 and 36 has been rejected as lacking enablement for a genus of antibodies that inhibit complement activation more than 50% at a molar ratio of 1:2 (antibody to C2). The Office asserts that it would require undue experimentation to make antibodies that satisfy the breadth of the claimed genus or to determine the conditions which any particular antibody might satisfy the claimed limiations. Applicants respectfully traverse this rejection.

In view of the discussion in Section I above, Applicants submit that they have clarified the conditions under which a given antibody would have greater than 50% inhibition at molar ratio of 1:2. The assay is easily performed and does not require undue experimentation. Applicants have taught how to make anti-C2 antibodies having

significant affinity for C2 and able to significantly inhibit complement activation. They have provided at least one example of this genus of antibodies and this example is representative of the entire genus. And though Applicants have not tested the other antibodies listed in Figure 2 for the binding ratio, these other antibodies may also perform at a ratio 1:2. Applicants aren't required to provide any examples, but have provided at least one example representative of the entire genus.

The USPTO has recognized that antibody technology is a mature technology where the level of skill is high and advanced. The art-recognized methods of making antibodies to a known characterized target are routine and do not require undue experimentation nor are these methods unpredicatable.

Thus, contrary to the Office's assertion, the quantity of experimentation is not undue, the art is not unpredicatable, the guidance provided is sufficient, and the assays and methods are known and routine. Therefore, Applicants submit that the full breadth of the claims are enabled and the rejection should be withdrawn.

III. Rejection Under 35 U.S.C. § 112, Second Paragraph

Claims 25, 26, and 27 have been rejected as failing to particularly and distinctly claim that which Applicants regard as their invention. Applicants have amended claims to reflect a deposited cell line rather than a deposited antibody. In view of this amendment, Applicants request that the rejection be withdrawn.

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Conclusion

In view of the foregoing amendments and remarks, Applicants submit that the claims are in condition for Allowance and request Rejoinder of Claims 28-30 and 32-35. Applicants request that the Examiner call the undersigned to address any issues regarding the Rejoined claims to bring the Application into condition for Allowance.

Respectfully Submitted,

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